

## REMARKS

Claims 1-35 and 37-43 will remain in the application for further prosecution. Claims 1-11, 18, 19, 20, and 21 have been amended to further distinguish the present invention from the cited references, which are discussed below.

### **Rejections Under 35 U.S.C. 112**

Claims 6-20 have been rejected under 35 U.S.C. 112 as indefinite for not positively stating a manipulation step.

Although these claims further define the method of the invention, it should be understood that the Applicants' method requires that it is carried out within a device having defined physical parameters. Note the following excerpts from the specification:

- “Mixing of liquids results when they enter and leave chambers that are large relative to the narrow channels through which they enter and leave”. ([0018] in the published application or page 5, lines 22-23)
- “Each of the two chambers is larger than the total volume of the liquids being mixed.” ([0020] in the published application or page 6, lines 14-15).
- “The depth of each chamber is sufficient to provide free space above the liquids after they have entered the chamber”. ([0020] in the published application or page 6, lines 16-17)
- “The capillary passageways preferably are located in the free space above the liquid in the chambers” ([0020] in the published application or page 6, lines 21-22)
- “...as liquids enter and exit capillaries connecting relatively large chambers it is probable that some localized eddies or disturbances are created as liquids speed up or

slow down and flow around distinct edges.” ([0041] in the published application or page 13, lines 21-24)

- “The liquids will be accelerated and decelerated as they move from their initial positions through capillaries into large chambers. It has been observed that droplets often form as the liquids exit from capillaries.” ([0041] in the published application or page 14, lines 2-4)
- “The difference in dimensions between those of the capillary passageways and the associated chambers is so large that the movement of liquids from one chamber to another creates a disturbance in the flow.” ([0043] in the published application or page 15, lines 13-15)

It should be clear that in describing the Applicants’ method one necessarily must include a description of important features of the device. Consequently, the Examiner is asked to reconsider his rejection, considering the above amendments to Claim 1.

Claims 25-28, 29-30, and 36 [sic] also have been rejected under 35 U.S.C. 112 as indefinite. Claim 36 was canceled in the previous amendment, obviating its rejection. Claim 21 has been amended to define the volume of the chambers with regard to the liquid well volumes. It should now be clear that the volume of the chambers can be determined since they are related to the volume of the liquids to be mixed.

#### **Rejections Under 35 U.S.C. 102**

Claims 1-4, 20, 21-22 and 24 have been rejected under 35 U.S.C. 102(e) as anticipated by Koop et al (“Koop”) U.S. 6,457,854. The Applicants do not agree that Koop anticipates these claims, since Koop discloses a very different device and method. Koop contains no first and

second chambers, connected through one or more separated capillary passageways. Instead, Koop uses two passageways that intersect many times to mix two liquids.

The Koop device evidently is intended to operate with continuous introduction of two liquids and with the device full of liquids. This can be seen in the following.

- Column 1, line 64 to column 2, line 9

Heat exchange to control temperature throughout the device implies continuous flow; while a device that operates in a batch manner without being completely filled with liquid would not provide temperature control.

- Column 2, lines 38-40 and lines 47-48

Referring to inlet passages supplying two phases implies continuous flow to produce a mixed phase, which is then removed through an outlet passage. The Koop device could not mix two phases if they were not continuously flowing.

- Column 2, lines 59-62

Two phase flows crossing one another and divided a number of times clearly refers to continuous flow of both phases.

- Column 3, lines 26-34

Reference to heat exchangers, pumps, and/or other process engineering components also implies continuous flow, with a completely filled device, or otherwise components could not be effective.

In contrast with the Koop device, it should be evident that the Applicant's device inherently operates in a batch manner without being completely filled. It should be obvious from

Figures 1a and 2a that fixed liquid volumes determined by wells 10 and 14 are dispensed from these wells by overcoming stops 12 and 16 and directed into chamber 18 to create a degree of mixing. The mixing process is completed by forcing the combined liquids into a second chamber through one or more capillary passageways. Advantageously, the chambers are larger than the amount of liquids being mixed. That is, the device is not filled. Furthermore, the Applicant's device is particularly useful as an analytical device, which inherently receives a fixed volume of a liquid sample and brings it into contact with a second liquid e.g. a reagent, a diluent, a conditioning agent and the like. Thus, it should be evident that the Applicant's device is, not only physically differs from Koop's, but operates differently. It cannot be seen how the Koop device could be operated in a batch manner, as the Applicants does (note the discussion at "Microfluidics Analytical Devices").

The Examiner contends that "a disclosed batch mode has not been claimed in the method steps nor such feature is supported in the apparatus claims." The Applicants disagree, but have further amended the claims to distinguish the Koop reference. It should be clear that the Applicants' method and device are intended to combine fixed volumes of liquids, such as a sample liquid with a conditioning agent. Thus, the Applicants' claims must refer to a batch procedure and not to a continuous flow of liquids, as in the Koop device.

Koop has been shown above to have intended to operate his mixing device with the continuous introduction of two liquids and with the device full of liquids. The structure shown in Koop could not be used in a batch manner, since there are no inlet wells to hold defined volume of the liquids to be mixed. Furthermore, Koop lacks chambers that receive the combined liquids. Note that he says that there is "a substantially equal passage cross-section in all areas of

the passage.” (column 2, lines 18-19). Therefore, the two liquids can never occupy a chamber that is larger than the volume of the liquids (as in amended claims 1 and 21).

The Examiner now attempts to interpret Koop as having a series of mixing chambers connected by two passageways. However, as indicated in the quotation from column 2, and from the drawings, Koop’s device contains uniform size passageways throughout, and therefore it does not correspond to the Applicants’ device. Consequently, Koop does not disclose the inventions as claimed.

**Rejection Under 35 U.S.C. 103**

Claims 3, 6-16, 18-19, 23, 25-35, 38, 40, and 42-43 have been rejected under 35 U.S.C. 103(a) as unpatentable (i.e. obvious) over Koop. Each of these claims depends from independent Claims 1 or 21 and should be allowable if the independent claims are allowed. The Applicants contend that Claims 1 and 21 are not anticipated by Koop and that they are not obvious. If Koop teaches forcing two liquids into intersecting sinusoidal passages, it does not follow that one skilled in the art would substitute two chambers connected by one or more separated capillary passageways, since laminar flow would be expected.

The subject matter claimed in dependent claims 3, 6-16, 18-19, 23, 25-35, 38, 40, and 42-43 does not involve optimum values reached by routine skill in the art, since the two devices are very different. Optimizing Koop, who teaches a very different mixing device, cannot be considered to produce the Applicants’ device.

Claims 5, 17, 37, 39, and 41 have been rejected under 35 U.S.C. 103(a) as unpatentable over Koop in view of Jakajima et al [sic] (Nakajima). The deficiencies of Koop have already been discussed. Nakajima described an improved device to create microspheres, which involved

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structures that are far different from those of the Applicants' device. The Examiner relies on "obvious to one skilled in the art" to combine Nakajima with Koop. However, there is no suggestion anywhere that combining Nakajima with Koop would yield the Applicants' invention.

Many additional references were cited, but not applied against the present claims. None of these are believed to be more pertinent than those used by the Examiner. Many of these patents involve movement or separation of liquids by electromotive means, rather than mixing of liquids. Hillman et al discusses microfluidic devices in which liquids are moved by capillary action and mentions the use of sonication for mixing and vanes to create turbulence.

The Examiner is asked to enter the proposed amendments, reconsider his rejection, and allow the amended claims. If further amendment is believed necessary, the Examiner is invited to contact the Applicants' attorney, at the telephone number provided below.

Respectfully submitted,

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Date

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